The SAMe-TT2R2 Score Predicts Poor Anticoagulation Control in AF Patients: A Prospective "Real-World" Inception Cohort Study

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The SAMe-TT_2R_2 score predicts poor anticoagulation in atrial fibrillation patients initiating Vitamin K antagonists: A prospective "real world" inception cohort study

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ABSTRACT

Background International guidelines recommend that an average individual time in therapeutic range should be >65-70% for optimal efficacy and safety outcomes whilst on a vitamin K antagonists (VKA). The SAMe-TT_2R_2 score would help decision making by identifying those newly diagnosed atrial fibrillation patients that could do well on vitamin K antagonists.

Objective To validate the predictive value of the SAMe-TT_2R_2 score for discriminating those who would achieve a high time in therapeutic range(≥65%) in a prospective 'real world' cohort of atrial fibrillation patients initiating oral anticoagulation therapy with VKA.

Methods We studied an inception cohort of consecutive non-valvular atrial fibrillation patients that initiated oral anticoagulation in our outpatient anticoagulation clinic. Baseline SAMe-TT_2R_2 score was calculated. At 6 months, we calculated time in therapeutic range using the Rosendaal method.

Results We included 459 patients: 222 (47%) male, median age 76 (interquartile range70-82); Median CHA_2DS_2-VASc score was 4 (3-5) and medianHAS-BLED score was 3 (2-3). Median SAME-TT_2R_2 score was 2 (1-2).

At 6 months, the mean ± standard deviationtime in therapeutic range at was 64±17% overall, and 248 (54%) patients had a time in therapeutic range value >65%. Patients with a SAME-TT_2R_2 score 0-1 had a mean time in therapeutic range of 67±18% whereas in patients with a SAME-TT_2R_2score ≥2, mean time in therapeutic range was 61±16%, p<0.001. The odds ratio (OR) for having a low time in therapeutic range value was 2.10 (95%CI 1.44-3.06, p<0.001) for those patients with a SAME-TT_2R_2 score ≥2.

Conclusions In a prospective 'real world' inception cohort of atrial fibrillation patients initiating oral anticoagulation with acenocoumarol, we have validated the clinical value of the SAME-TT_2R_2 score, for the identification of patients who would have poor quality anticoagulation. Thus, rather than imposing a 'trial of vitamin K antagonists' for such patients (and exposing such patients to thromboembolic risks), we can *a priori* identify those patients who can (not cannot) do well on a vitamin K antagonists. Such patients

would benefit from additional strategies for improving anticoagulation control with VKAor alternative oral anticoagulant drugs.

Key words: time in therapeutic range, acenocoumarol, atrial fibrillation, anticoagulation

INTRODUCTION

Atrial fibrillation is associated with high morbidity and mortality, with an increased risk of stroke and thromboembolism[1]. Oral anticoagulation is highly effective reducing the risk of stroke and mortality, compared to placebo/control [2]. However, the efficacy and safety of VKA depends upon the quality of anticoagulant control, as reflected by the average percentage of the time in therapeutic range of INR 2.0-3.0. Various studies have shown how a high time in therapeutic range translates into a lower risk of stroke and bleeding, whilst on oral anticoagulation[3-5]. A recent European consensus document recommends that an average individual time in therapeutic range should be >70% for optimal efficacy and safety outcomes whilst on a vkaS[6,7] and this is also recommended in the European Guidelines for the management of AF[8]. In the National Institute for Health and Care Excellence (NICE) guidelines, a time in therapeutic range of >65% is recommended for patients with atrial fibrillation who are taking VKA therapy [9].

In 2013, Apostolakis et al. [10]proposed and validated the SAMe-TT_2R_2 score [**S**ex, **A**ge (<60 years), **Me**dical history (at least 2 of the following: hypertension, diabetes, coronary artery disease/myocardial infarction, peripheral arterial disease, congestive heart failure, previous stroke, pulmonary disease, hepatic or renal disease), **T**reatment (interacting drugs eg. amiodarone for rhythm control) [all 1 point], as well as current **T**obacco use (2 points) and **R**ace (non-Caucasian; 2 points)]. This simple clinical score (SAMe-TT_2R_2) could help decision making by identifying those atrial fibrillation patients that would probably do well on VKAs with a high average time in therapeutic range (ie. those with SAMe-TT_2R_2 score<2).

We have recently validated this score in a retrospective analysis of our "real world" anticoagulated atrial fibrillation patients[11]. Also, a high SAMe-TT_2R_2 score (reflecting poor anticoagulation control with poor time in therapeutic range) was associated with more bleeding, adverse cardiovascular events and mortality during follow-up. Prior validation studies [11-13] have been made on retrospective analysis of clinic or hospital cohort studies, and thus, the objective of the present study was to validate *a priori* the use of the SAMe-TT_2R_2 score in a contemporary inception cohort of anticoagulation-

naïve atrial fibrillation patients who were prospectively initiating oral anticoagulation with a vitamin K antagonist, acenocoumarol.

METHODS

We included consecutive non-valvular atrial fibrillation patients that initiating oral anticoagulation with acenocoumarolin our out-patient anticoagulation clinic, between January and December 2013, who maintained oral anticoagulation and were followed up prospectively for 6 months, for this study. This inception cohort of patients was anticoagulation-naïve at baseline.

A complete medical history was recorded at inclusion. Baseline stroke risk was assessed using the CHA_2DS_2-VASc [Cardiac failure or dysfunction, Hypertension, Age over 75 years [Doubled], Diabetes, Stroke [Doubled] – Vascular disease, Age between 65-74 and Sex category [Female]) score, as described in recent guidelines[8,14]. The HAS-BLED bleeding risk score was calculated as a measure of baseline bleeding risk, as the result of adding one point to hypertension, abnormal renal/liver function (one point each), stroke, bleeding history or predisposition, labile INR, elderly (age over 65) and drugs/alcohol concomitantly (one point for each one)[15].

At baseline SAMe-TT_2R_2 score was calculated as previously described [10]. At six months we calculated time in therapeutic range using the established Rosendaal method[16]. Once the patient reached steady dose, the frequency of INR testing was once a month, so all patients had a minimum of 8 visits.

Exclusion criteria

Patients with valvular atrial fibrillation (prosthetic or not) were excluded. We also excluded those patients that did not receive at least 6 months oral anticoagulation treatment, those suffered from any event leading to temporarily discontinue oral anticoagulation, as this would influence achievement of stable anticoagulation.

Statistical analysis

Continuous variables were tested for normality by the Kolmogorov-Smirnov test. Continuous variables are presented as a mean ± SD or median (interquartile range), as appropriate, and categorical variables as a percentage. Differences were compared using the student t-test or Mann-Whitney test, as appropriate. The association between SAMe-TT_2T_2 score and low time in therapeutic range (<65%) was assessed by logistic regression model. A $P < 0.05$ was accepted as statistically significant. Statistical analyses were performed using SPSS 15.0 for Windows (SPSS, Inc., Chicago, Ill).

RESULTS

During January to December 2013, 719 consecutive patients with non-valvular atrial fibrillation were initiated on oral anticoagulation with acenocoumarol in our out-patient anticoagulation clinic. This anticoagulation clinic serves a population of 500,000 and approximately 7,500 patients are treated annually (of these, 62% are patients with atrial fibrillation). Based on our study inclusion/exclusion criteria, only 459 patients (64% of the whole cohort) entered the final analysis [Table 1]. The reasons for exclusion patients were as follows: 74 patients (28%) needed interruption for surgical intervention or any other invasive procedure; in 73 (28%) patients their primary care doctor stopped oral anticoagulation for several reasons (advanced age, patient preference); 51 (20%) patients stopped oral anticoagulation one month after effective cardioversion; 44 patients were moved to another anticoagulation clinic (17%); and 18 (7%) patients changed to a Non-vitamin K antagonists antagonist Oral Anticoagulant (NOAC, previously referred to as new or novel oral anticoagulant) before reaching 6 months of anticoagulation treatment with VKAs (see flowchart, figure 1)

Our 459 patients included 222 (47%) males, with median age 76 (interquartile range, IQR 70-82), median CHA_2DS_2-VASc score of 4 [IQR 3-5; whereby 92% with CHA_2DS_2-VASc score≥2] and median HAS-BLED score of 3 (IQR 2-3); 54% with HAS-BLED score ≥3.

Median SAMe-TT_2R_2 score was 2 (IQR 1-2) and 55% patients had a score <2. Only 18 patients had a score >3. Overall the mean time in therapeutic range at six months was 64±17%, and 248 patients (54%) had a time in therapeutic range value >65%.

After a follow-up of 6 months, patients with a SAMe-TT_2R_2 score <2 had a mean time in therapeutic range value of 67±18% compared to a mean time in therapeutic range of 61±16% amongst patients SAMe-TT_2R_2 score ≥2 [p=0.001]. The odds ratio (OR) for having a low time in therapeutic range for patients with a SAMe-TT_2R_2 score ≥2 was 2.10 (95%CI 1.44-3.06, p<0.001).

There was no relationship between time in therapeutic range values at 6 months and thrombotic risk based on a CHA_2DS_2-VASc categorisation of <2 and ≥2, with mean TTRs of 64±17% vs 67±17%, respectively (p=0.232). For the HAS-BLED score, patients with a score <3 had a mean time in therapeutic range of 66±17% vs patients with HAS-BLED ≥3, who had a mean time in therapeutic range value of 63±17% (p=0.08).

DISCUSSION

In this study, we validated for the first time the value of SAMe-TT_2R_2 score in a large consecutive "real world" inception cohort of patients who were initiating oral anticoagulation. As our patients were on acenocoumarol, or paper gives an additional use of the SAMe-TT_2R_2score for this VKA drug, which is the second most commonly used coumarin (after warfarin) in the world.Based on our analysis, patients with a high SAMe-TT_2R_2 score (≥2) would have a 2 fold increased risk for suboptimal quality of oral anticoagulation, as assessed by a low time in therapeutic range value at 6 months after initiating treatment with a vitamin K antagonist.

Despite the NOACs[17] being increasingly used, the VKAsremain the main oral anticoagulation used in many countries, especially where economic considerations are a factor. One criterion often used to sanction NOAC use is a time in therapeutic range value at 6 months <65% [9,17]. Thus, many patients have to undergo a 'trial of vitamin K antagonist' (or 'warfarin stress test') to show that high time in therapeutic range cannot be achieved, before a NOAC is allowed.

Thus, use of a simple score based on clinical risk factors allows the clinician to make an informed decision whether a non-anticoagulated atrial fibrillation patient is likely (or not) to do well on a vitamin K antagonist. This is relevant since average time in therapeutic range may be poor or suboptimal in inception cohorts for as long as 6 months (being an average of 47% in one recent US study)[18], and this may translate into worse thromboembolic outcomes in this inception phase, being increased by 70%[19]. Those patients with a high SAMe-TT_2R_2 can be justifiably started on a NOAC up front (without a 'warfarin stress test') or be targeted for additional interventions (eg. more intense education, regular review and follow-up, etc[20]) whilst those patients with a SAMe-TT_2R_2 score <2 can be started on a vitamin K antagonist, as they are likely to do well. Such an approach is illustrated in Figure 2.

The efficacy and safety of therapy is closely associated to the quality of oral anticoagulation management[6,11]. These patients are best managed in specialized anticoagulation clinics, which achieves higher values of time in therapeutic range and provides the best outcomes[6,18-22]. Even in clinical trials, patients in centres with high

average time in therapeutic range may have less profound differences in efficacy outcomes between NOACs and warfarin[23]. The maintenance dose of VKA is influenced by many different factors, including race, dietary vitamin K intake, comorbidities (eg. liver disease and acute illness) or whether the patient may be taking interacting drugs[24]. The average individual time in therapeutic range generally increases over time, but even in very well and experienced patients, their time in therapeutic range value can decrease during follow-up[11]. This is especially important in patients who initiate conventional oral anticoagulation more INR fluctuations occur during the first 3 months[24]. In our cohort, for example, we found that the average time in therapeutic range value at 6 months was 64% and only 49% had a time in therapeutic range value up to 65%.

It is important to note that our study was performed using acenocoumarol as vitamin K antagonist drug. Compared to warfarin, acenocoumarol has a shorter half life, about 8 hours[25]. Hence, patients taking acenocoumarol may be more likely to have unstable anticoagulation control than those taking warfarin[26]. In addition, acenocoumarol has been related with a higher risk for bleeding than warfarin[22]. Thus, use of the SAMe-TT_2R_2 score in this population taking acenocoumarol as their drug may confer additional advantages.

Prediction algorithms (including clinical and genetic data) for VKA treatment could also be another option[27]. However the use of these algorithms in clinical practice remains uncertain, given the contradictory results of two controlled trials of genotype-guided dosing[28-30]. In contrast to complex (and expensive) genotyping, we have now prospectively validated the use of an easy, simple and cheap score that would detect which atrial fibrillation patients are likely to do well on vitamin K antagonists(with good average time in therapeutic range).This is important since even small differences in time in therapeutic range could translate to lower risk of adverse events whilst on VKA[5].

Limitations

We only included in those patients that continued treatment during the initial 6 months, so some very high risk patients that suffer from acute events during the first months may have been excluded. Given our small sample size and followup duration,

we would have been underpowered to examine thromboembolic and bleeding events in this cohort. Also, the proportion of patients with a very high SAMe-TT_2R_2score (>3) was low. All patients included were Caucasian, who were managed in a dedicated anticoagulation clinic, where the average overall time in therapeutic range was reasonably good, at 64% time in therapeutic range.

We made reference to NICE guidelines criteria for defining good time in therapeutic range (≥65%) as this was based following a comprehensive evidence synthesis and appraisal, as well as cost effectiveness[9]. They also considered poor anticoagulation control as defined by 2 INR values higher than 5 or 1 INR value higher than 8 within the past 6 months, 2 INR values less than 1.5 within the past 6 months or time in therapeutic range less than 65%; however, we did not perform these additional measures within our cohort.

Finally, another limitation is the possibility that low time in therapeutic range could be due to low adherence to treatment, which would also affect the further treatment with NOACs if they would be used. However, patients regularly attended the anticoagulation clinic and were reviewed by nurses if INR was out of range.

Conclusion

In a prospective 'real world' inception cohort of anticoagulation-naïve patients initiating oral anticoagulation with acenocoumarol, we have validated the clinical value of the SAMe-TT_2R_2score, for the identification of which patients would have poor quality anticoagulation. These patients would benefit from additional strategies for improving anticoagulation control with VKA or alternative oral anticoagulant drugs.

REFERENCES

1. Wolf PA AR, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. *Stroke.* 1991;22:983-988.
2. Hart RG PL, Aguilar MI. Meta-analysis: antithrombotic therapy to prevent stroke in patients who have nonvalvular atrial fibrillation. *Ann Intern Med* 2007;146:857-867.
3. Gallagher AM, Setakis E, Plumb JM, Clemens A, van Staa TP. Risks of stroke and mortality associated with suboptimal anticoagulation in atrial fibrillation patients. *Thrombosis and haemostasis.* 2011;106(5):968-977.
4. Morgan CL, McEwan P, Tukiendorf A, Robinson PA, Clemens A, Plumb JM. Warfarin treatment in patients with atrial fibrillation: observing outcomes associated with varying levels of INR control. *Thrombosis research.* 2009;124(1):37-41.
5. Wan Y, Heneghan C, Perera R, et al. Anticoagulation control and prediction of adverse events in patients with atrial fibrillation: a systematic review. *Circulation. Cardiovascular quality and outcomes.* 2008;1(2):84-91.
6. De Caterina R HS, Wallentin L, Andreotti F, Arnesen H, Bachmann F, Baigent C, Huber K, Jespersen J, Kristensen SD, Lip GY, Morais J, Rasmussen LH, Siegbahn A, Verheugt FW, Weitz JI. . Vitamin K antagonists in heart disease: current status and perspectives (Section III). Position paper of the ESC Working Group on Thrombosis--Task Force on Anticoagulants in Heart Disease. . *Thrombosis and haemostasis.* 2013;110:1087-1107.
7. Gallego P, Roldan V, Marin F, et al. Cessation of oral anticoagulation in relation to mortality and the risk of thrombotic events in patients with atrial fibrillation. *Thrombosis and haemostasis.* 2013;110(6):1189-1198.
8. Camm AJ, Lip GY, De Caterina R, et al. 2012 focused update of the ESC Guidelines for the management of atrial fibrillation: an update of the 2010 ESC Guidelines for the management of atrial fibrillation--developed with the special contribution of the European Heart Rhythm Association. *Europace : European pacing, arrhythmias, and cardiac electrophysiology : journal of the working groups on cardiac pacing, arrhythmias, and cardiac cellular electrophysiology of the European Society of Cardiology.* 2012;14(10):1385-1413.
9. National-Institute-for-Health-and-Care-Excellence. Atrial fibrillation: the management of atrial fibrillation. (Clinical guideline 180.). http://guidance.nice.org.uk/CG180. 2014. Last access 20/04/2015
10. Apostolakis S, Sullivan RM, Olshansky B, Lip GY. Factors affecting quality of anticoagulation control among patients with atrial fibrillation on warfarin: the SAMe-TT(2)R(2) score. *Chest.* 2013;144(5):1555-1563.
11. Gallego P, Roldan V, Marin F, et al. SAME-TTR score, time in therapeutic range and outcomes in anticoagulated patients with atrial fibrillation. *The American journal of medicine.* 2014.
12. Poli D, Antonucci E, Testa S, Lip GY. A prospective validation of the SAME-TT2R 2 score: how to identify atrial fibrillation patients who will have good

anticoagulation control on warfarin. *Internal and emergency medicine.* 2014;9(4):443-447.

13. Lip GY, Haguenoer K, Saint-Etienne C, Fauchier L. Relationship of the SAMe-TT(2)R(2) score to poor-quality anticoagulation, stroke, clinically relevant bleeding, and mortality in patients with atrial fibrillation. *Chest.* 2014;146(3):719-726.
14. Lip GY, Nieuwlaat R, Pisters R, Lane DA, Crijns HJ. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the euro heart survey on atrial fibrillation. *Chest.* 2010;137(2):263-272.
15. Pisters R, Lane DA, Nieuwlaat R, de Vos CB, Crijns HJ, Lip GY. A novel user-friendly score (HAS-BLED) to assess 1-year risk of major bleeding in patients with atrial fibrillation: the Euro Heart Survey. *Chest.* 2010;138(5):1093-1100.
16. Rosendaal FR, Cannegieter SC, van der Meer FJ, Briet E. A method to determine the optimal intensity of oral anticoagulant therapy. *Thrombosis and haemostasis.* 1993;69(3):236-239.
17. Husted S dCR, Andreotti F, Arnesen H, Bachmann F, Huber K, Jespersen J, Kristensen SD, Lip GY, Morais J, Rasmussen LH, Siegbahn A, Storey RF, Weitz JI; ESC Working Group on Thrombosis Task Force on Anticoagulants in Heart Disease. . Non-vitamin K antagonist oral anticoagulants (NOACs): No longer new or novel. *Thrombosis and haemostasis.* 2014;111.
18. Dlott JS, George RA, Huang X, et al. National assessment of warfarin anticoagulation therapy for stroke prevention in atrial fibrillation. *Circulation.* 2014;129:1407-1414.
19. Azoulay L, Dell'Aniello S, Simon TA, Renoux C, Suissa S. Initiation of warfarin in patients with atrial fibrillation: early effects on ischaemic strokes. *European heart journal.* 2014;35:1881-1887.
20. Clarkesmith DE, Pattison HM, Lip GY, Lane DA. Educational intervention improves anticoagulation control in atrial fibrillation patients: the TREAT randomised trial. *PloS one.* 2013;8(9):e74037.
21. Ansell J, Hollowell J, Pengo V, Martinez-Brotons F, Caro J, Drouet L. Descriptive analysis of the process and quality of oral anticoagulation management in real-life practice in patients with chronic non-valvular atrial fibrillation: the international study of anticoagulation management (ISAM). *Journal of thrombosis and thrombolysis.* 2007;23(2):83-91.
22. Palareti G, Cosmi B. Bleeding with anticoagulation therapy - who is at risk, and how best to identify such patients. *Thrombosis and haemostasis.* 2009;102(2):268-278.
23. Wallentin L, Yusuf S, Ezekowitz MD, et al. Efficacy and safety of dabigatran compared with warfarin at different levels of international normalised ratio control for stroke prevention in atrial fibrillation: an analysis of the RE-LY trial. *Lancet.* 2010;376(9745):975-983.
24. Garcia DA, Lopes RD, Hylek EM. New-onset atrial fibrillation and warfarin initiation: high risk periods and implications for new antithrombotic drugs. *Thrombosis and haemostasis.* 2010;104(6):1099-1105.

25. Beinema M, Brouwers JR, Schalekamp T, Wilffert B. Pharmacogenetic differences between warfarin, acenocoumarol and phenprocoumon. *Thrombosis and haemostasis.* 2008;100(6):1052-1057.
26. Palareti G, Legnani C, Guazzaloca G, et al. Risks factors for highly unstable response to oral anticoagulation: a case-control study. *British journal of haematology.* 2005;129(1):72-78.
27. Cerezo-Manchado JJ, Rosafalco M, Anton AI, et al. Creating a genotype-based dosing algorithm for acenocoumarol steady dose. *Thrombosis and haemostasis.* 2013;109(1):146-153.
28. Verhoef TI, Ragia G, de Boer A, et al. A randomized trial of genotype-guided dosing of acenocoumarol and phenprocoumon. *The New England journal of medicine.* 2013;369(24):2304-2312.
29. Pirmohamed M, Burnside G, Eriksson N, et al. A randomized trial of genotype-guided dosing of warfarin. *The New England journal of medicine.* 2013;369(24):2294-2303.
30. Kimmel SE, French B, Kasner SE, et al. A pharmacogenetic versus a clinical algorithm for warfarin dosing. *The New England journal of medicine.* 2013;369(24):2283-2293.

Table 1. Baseline clinical characteristics

Baseline characteristics	N= 459
Male sex, n(%)	222 (47%)
Age, median (IQR) Age < 60	76 (70-82) 38 (8%)
Hypertension	368 (80%)
Diabetes mellitus	141 (31%)
Heart failure	87 (19%)
History of stroke or TIA	67 (15%)
Peripherical embolism	23 (5%)
Hepatic impairment	12 (3%)
Renal impairment	51 (11%)
Coronary artery disease	70 (15%)
Hypercholesterolemia	186 (41%)
Chronic obstructive pulmonary disease	50 (11%)
Current smoking habit	38 (8%)
Previous bleeding episode	37 (8%)
Concomitant treatment *Amiodarone* *Calcium antagonist* *Beta-blockers* *Digoxin*	 72 (16%) 44 (10%) 273 (59%) 33 (7%)
CHA_2DS_2-VASc score, median (IQR)	4 (3-5)
HAS-BLED score, median (IQR)	3 (2-3)
SAME-TT_2R_2 score, median (IQR)	2 (1-2)

CHA_2DS_2-VASc: Cardiac failure or dysfunction, Hypertension, Age ≥75y [Doubled], Diabetes, Stroke [Doubled] – Vascular disease, Age 65-74y and Sex category [Female]

HAS-BLED: Hypertension, Abnormal Renal/Liver Function, Stroke, Bleeding History or Predisposition, Labile INR, Elderly, Drugs/Alcohol Concomitantly

SAMe-TT_2R_2: Sex, Age (<60 years), Medical history (at least 2 of the following: hypertension, diabetes, coronary artery disease/myocardial infarction, peripheral arterial disease, congestive heart failure, previous stroke, pulmonary disease, hepatic or renal disease), Treatment (interacting drugs e.g. amiodarone for rhythm control) [all 1 point], as well as current Tobacco use (2 points) and Race (non-Caucasian; 2 points)

Figure 1

Flowchart of patient selection

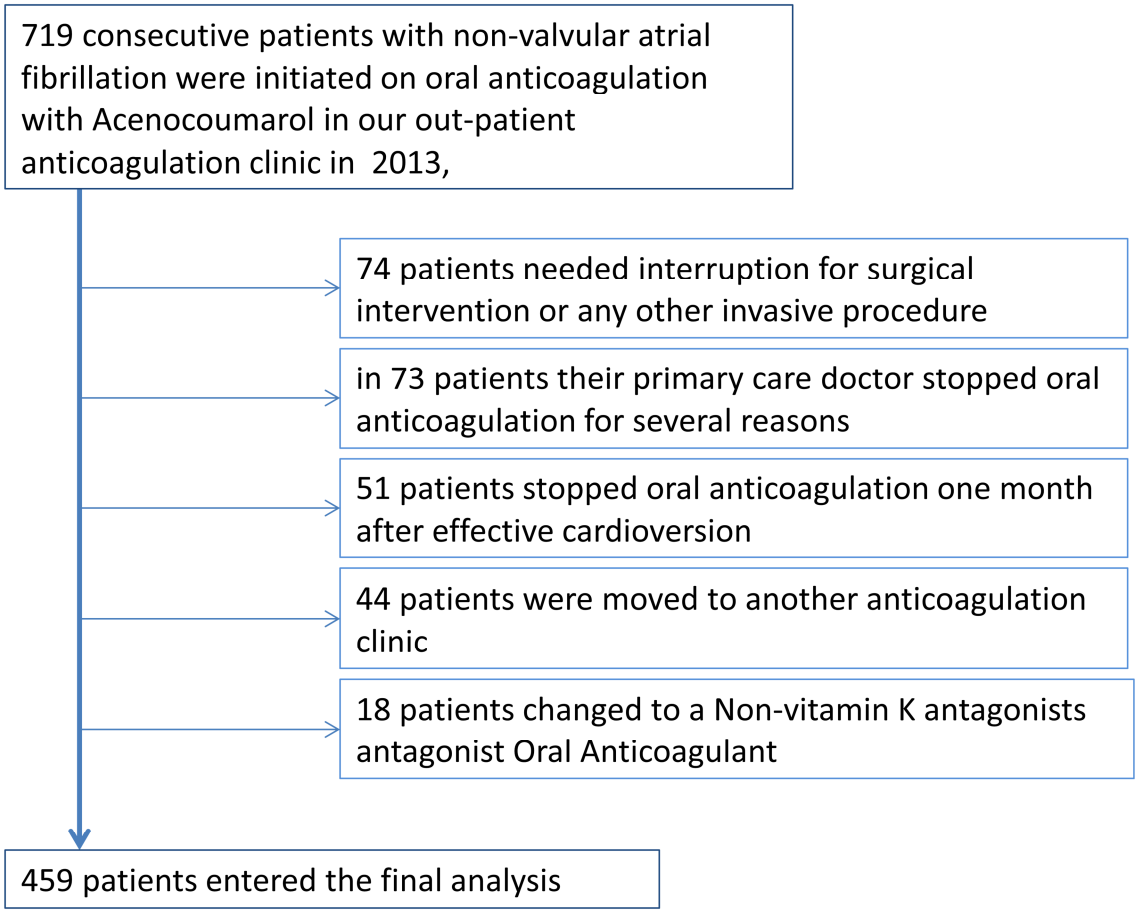
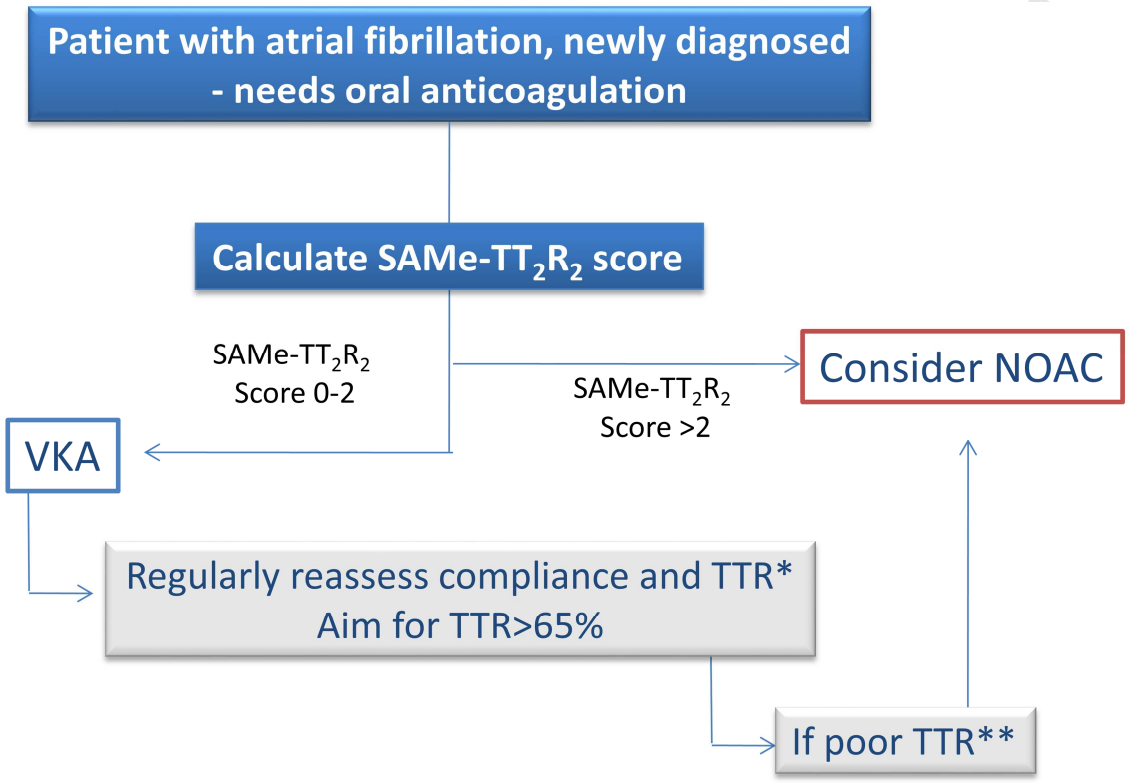


Figure 2

Incorporation of the SAME-TT_2R_2 score into clinical decision making for anticoagulation therapy in newly diagnosed anticoagulation-naïve patients with atrial fibrillation



NOAC: non-vitamin K antagonist oral anticoagulant
TTR: time in therapeutic range
VKA: vitamin K antagonist
*When calculating TTR, use a validated method (eg. Rosendaal method for computer-assisted dosing) or proportion of test in range for manual dosing
** Reasses for poor anticoagulation control

CLINICAL SIGNIFICANCE

- In a prospective 'real world' inception cohort of AF patients initiating oral anticoagulation with acenocoumarol, we have validated the clinical value of the SAME-TT_2R_2 score, for the identification of patients who would have poor quality anticoagulation.
- We can identify those patients who can (not cannot) do well on a VKA. Such patients would benefit from additional strategies for improving anticoagulation control with VKA or alternative oral anticoagulant drugs.